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LETTER TO THE EDITOR

Dear Sir,

We were interested to read the paper by Price et al. (2004;98:17–24) which purported to show an association between antibiotic prescribing trends in general practice and community-acquired pneumonia mortality. We are concerned that there are serious methodological flaws in this paper which we would like to bring to your attention.

The endpoint used was imprecise and potentially inaccurate. The title of the paper refers to community-acquired pneumonia mortality. The source for this was death certificate data for England and Wales with pneumonia as the cause of death, excluding cases where this was a consequence of underlying disease. As the authors acknowledge, diagnosis of pneumonia outside hospital is difficult both in life and at death. Death certificate data will include not only community-acquired pneumonia, but also an unknown number of cases of hospital-acquired pneumonia, aspiration pneumonia and pneumonias in the immunocompromised and also other non-pneumonia respiratory conditions where general practitioner (GP) antibiotic prescribing is unlikely to have influenced outcome. In a study using death certificate data, with pneumonia as the 'Underlying Cause of Death' where the additional step of contacting the doctor responsible for care of the individual's final illness was taken, additional information was identified, not provided on the death certificate, that may have been relevant to the death, in 72% of cases.[1] In a separate study, national death certificate data from Scotland were found to overestimate true community-acquired pneumonia mortality by a factor of two, largely due to the use of the poorly defined label of 'bronchopneumonia' which was also included in the ICD9 pneumonia codes used by Price et al.[2]

Antibiotic prescribing data were obtained from a different population, a UK (not England and Wales) database for seventeen ICD10 (not Read as stated in the paper) codes that might be considered to reflect lower respiratory tract infection (LRTI). Only five of these were for pneumonia, with the majority likely to represent the condition that GPs label as acute bronchitis. Data were not age corrected. Of the 439 948 pneumonia deaths between January 1993 and December 2000, 95% were in the >64 years age group. This is the age group in which the smallest (maximum -5.9%) reduction in GP antibiotic prescribing has occurred (compared to a maximum of -26.1% in the <16 years age group).[3] Any association between antibiotic prescribing and pneumonia mortality must be based on prescribing in this older age group. We would suggest to the authors that they reanalyse pneumonia deaths and prescribing rates for LRTI in these age groups and exclude bronchopneumonia (ICD 9 code 485).

The statistical analysis considers only one time variable and should in addition to cyclical changes take account of secular changes and also should adjust for time-varying factors such as new initiatives. Data from the USA suggest that pneumonia mortality is increasing as part of a long-term trend which began before reductions in antibiotic prescribing began.[4] Interestingly, Figure 2 in the Price paper also suggests that the trend for a rise in pneumonia mortality had begun by 1995/1996 before changes in antibiotic prescribing occurred in 1997/1998. Additional data from before 1993/1994 would have been helpful, but any attempt to correct for death certificate coding changes would be likely to be inaccurate. The authors chose to use a constant 12-week period for all years. This will over- and underestimate if the winter mortality peaks did not fit neatly into this period each year. The use of an arbitrary constant of 85% to produce winter excess deaths means that in high summer mortality years, the absolute number of excess deaths could be lower in the winter than in a year with a very low summer mortality. It is difficult to know how standardization for influenza has been applied in a meaningful way. Standardization needs to be based on the age-specific incidence of illness since influenza epidemics are highly variable in their impact. Furthermore, incidence rates of influenza-like illness reported in the WRS are always considerably less than the rates of acute bronchitis regardless of age. Acute bronchitis in the elderly is highly consistent in the first few weeks of the year and consistently related to mortality peaks

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(all cause mortality) though January is not consistently the coldest month. There are considerable limitations when examining individual cause mortality in the oldest age groups in isolation from all cause mortality.

The authors have been somewhat selective in their use of references in the discussion. They cite three publications in support of delay in antibiotic prescribing being of prognostic importance in pneumonia. One of these was a review paper[5] and the other two were studies of hospitalized patients, not those managed by GPs in the community.[6,7] They rightly report that antibiotics have been shown to have a modest beneficial effect in controlled trials in acute bronchitis and go on to say that they are unlikely to cause harm in most LRTI patients. However, the most up to date version of their reference uses the term 'The magnitude of this benefit, however, is similar to that of the detriment from potential adverse effects' which gives a slightly different emphasis.[8] Benefit in the individual must, in addition be balanced against harm to the population, as is recognized to have occurred as a result of the development of antibiotic resistance in common bacterial pathogens due to inappropriate use of antibiotics in the community.

Data from other studies are at variance with those of Price et al. A study of the relationship between GP-diagnosed respiratory infections and antibiotic prescriptions using Prescription Pricing Authority all age and all cashed prescription data has shown that both have been falling since 1993.[9] Further analysis of this dataset shows the ratio of prescriptions for antibiotics (regardless of reason) to persons presenting with LRTI actually increased slightly over the period. This analysis took no account of antibiotic prescribing for skin and urinary tract infections, the incidence of which had not changed over the same period. Nevertheless, since antibiotic prescribing is dominated by respiratory infections the data do not suggest that doctors are prescribing less antibiotics for the patients who consulted.

Furthermore, there is strong evidence from a prospective study that decreasing antibiotic use for LRTI in adults does not result in increased office visits for pneumonia, never mind increased mortality.[10] This intervention was associated with a reduction in antibiotic use from 74% to 48%. There were 542 patients in the intervention phase so that 140 (26%) fewer patients received antibiotics. According to the analysis by Price et al. this should have resulted in one additional death from CAP. In fact, 0.7% of the intervention group had a return office visit for pneumonia, which was not significantly different from return visits for pneumonia in the control cohort (1.5%).

It is our opinion that the methods used in this publication do not support the conclusions reached. Whilst the authors have observed that deaths registered due to pneumonia have increased in recent winters they have not demonstrated that this is anything to do with prescribing for LRTI. Despite the care used by the authors to stress the association between results, there remains a suggestion of a causative link. Thus, these conclusions may be open to misinterpretation by the uninformed reader. As the authors state, recent initiatives have been directed at evidence-based antibiotic prescribing to reduce inappropriate prescribing and thus reduce the pressure that drives the development of antimicrobial resistance. We would be concerned if this had led to antibiotics not being prescribed to those for whom such prescription is appropriate and would welcome good evidence that this was or was not occurring. We do not consider that this paper is consistent with this, but accept and support the need for more robust research in this area.

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